

Antibiotic Susceptibility Patterns of Urinary Pathogens in Female Outpatients

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ABSTRACT

Background: Urinary tract Infection (UTI) is among the most common infections described in outpatient setting and hospital patients. In almost all cases empirical antimicrobial treatment initiates before the laboratory results of urine culture are available; thus antibiotic resistance may increase in uropathogens due to frequent use of antibiotics. **Aims:** The study was designed to find the prevalence of UTI in females with urinary tract symptoms, to determine the causative organism (s) of UTI, and to determine the antibiotic susceptibility pattern of microbial agents isolated from urine culture (antibiogram). **Materials and Methods:** The prospective, observational study involved 139 females, aged 15 years and above clinically suspected for UTI attending outpatient Departments of Vivekananda Polyclinic and Institute of Medical Sciences, Lucknow. A structured questionnaire was used to interview the study subjects. A chi-square test and Fisher Exact test were used to analyze data. **Results:** The overall prevalence of UTI was found to be 45.32% (63/139). *Escherichia coli* (33.1%) and *Klebsiella pneumoniae* (7.9%) were the most common organisms isolated. The most effective antibiotic for both was Nitrofurantoin. **Conclusions:** Regular monitoring is required to establish reliable information about susceptibility pattern of urinary pathogens for optimal empirical therapy of patients with UTI.

Keywords: Antimicrobial susceptibility patterns, Prevalence, Urinary tract infections

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Introduction

Urinary tract Infection (UTI) is one of the most common clinical syndromes encountered in general and gynecological practices.^[1] They are among the most common infections described in outpatients setting and hospital patients.^[2,3] Adult women (40–50%) have a history of at least one episode of UTI in their lifetime. The incidence of UTI among women rises by 5% per decade. There is an increase in UTI during pregnancy by about 7%.^[4] UTIs may be community acquired or nosocomial. Community acquired infection is caused by *Escherichia coli*, *Klebsiella pneumoniae*, *Proteus mirabilis*, *Staphylococcus*

saprophyticus or *Enterococcus faecalis*, while the hospital acquired ones are *Escherichia coli*, *Pseudomonas aeruginosa*, *Proteus sp*, *Enterobacter sp.*, *Serratia sp.* or *Enterococcus*.

UTI is a broad term that encompasses asymptomatic bacteriuria and symptomatic infection with microbial invasion and inflammation of the urinary tract. While up to 90% of the patients with UTIs complain of urinary tract symptoms, one third or more of the patients with these symptoms do not have bacteriuria.^[5] The most common symptoms for which most patients seek treatment are dysuria and frequency. Dysuria and frequency together raise the probability of UTI to more than 90%, effectively ruling in the diagnosis by history alone.^[6] In almost all cases of UTI, empirical antimicrobial treatment initiates before the laboratory results of urine culture are available; thus antibiotic resistance may increase in uropathogens due to frequent use of antibiotics.^[7] Increasing resistance in bacterial pathogens is of world-wide concern. The prevalence of antimicrobial resistance in patients with UTI is increasing and can vary according to geographical and regional location.^[8]

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For this reason, knowledge of the etiological agents of UTIs and their antimicrobial resistance patterns in specific geographical locations may aid clinicians in choosing the appropriate antimicrobial empirical treatment. The literature on prevalence of UTI among females in Lucknow was scarce in recent decades; thereby the present study was undertaken to find out the prevalence of UTI and to determine the antimicrobial susceptibility patterns of commonly used antibiotics among females in Lucknow.

Materials and Methods

This observational, prospective 12 months' study was carried out among out patient departments of Obstetrics and Gynaecology and Medicine of Vivekananda Polyclinic and Institute of Medical Sciences, Lucknow after ethical clearance from the institution review board. All females aged 15 years and above attending the respective outpatient departments clinically suspected for UTI were selected for the purpose of the study during the study period. The total number of females surveyed was 139. Patients who had no symptoms suggestive of UTI at the time of observation were excluded from the study. Females suffering from diabetes mellitus, renal disorders, HIV positivity, or on corticosteroid therapy were also excluded. Those females who did not give consent were noncooperative or refused to provide the necessary information were not included in the study.

The necessary information was collected using the interview technique from each respondent after informed consent. A structured questionnaire was used to assess the study subjects' self-reported information regarding socio-demographic characteristics and urinary symptoms. Data regarding organisms causing UTI and their antibiotic sensitivity patterns were collected.

All study subjects were advised to collect the mid-stream urine sample in wide-mouthed sterile containers. They were instructed to clean the area around the urethral opening with clean water, dry the area, and collect the urine with the labia held apart. Samples were processed within 1 hour of collection. For direct microscopy (wet film preparation) 50 μ l of well-mixed uncentrifuged urine was taken on a slide and a cover slip placed on it. It was viewed under a high-power objective. The presence of one pus cell/7 hpf was considered significant pyuria.^[9]

Jensens modification of gram staining was employed. At least 20 fields were examined and detection of one or more morphologically similar bacteria per oil immersion field was treated as significant. A mixture of *E. coli* and *Staphylococcus aureus* was used as a positive control and uninoculated broth as negative control. The presence

of more than two morphologically different organisms indicated the presence of mixed flora.

For urine culture the urine sample (1 μ l) was inoculated on cysteine lactose electrolyte deficient medium, using a standard loop of internal diameter 1.34 mm (semiquantitative method). The plates were read after 24 hours of aerobic incubation at 37°C. They were further incubated for another 24 hours before a negative report was issued. A single organism obtained in counts of >100,000 cfu/ml was further identified by standard biochemical techniques.^[9]

The agar diffusion technique was used for antibiotic susceptibility testing.^[9] Five colonies of the test organisms were streaked on agar plates using a sterile inoculating wire loop. The appropriate multidisk depending on whether the test organism plated will be gram negative or gram positive was then placed firmly onto the surface of the dried plates, using sterile forceps. The plates were left at room temperature for 1 hour to allow diffusion of the different antibiotics from the disk into the medium. The plates were further incubated at 37°C for 18–24 hours. Interpretation of results was done using the zone sizes. The zone of inhibition of greater than 10 mm was considered sensitive, 5–10 mm as moderately sensitive and no zone of inhibition as resistant.

The antibiotics tested were Amoxicillin, Ampicillin, Ampicillin-Sulbactam, Piperacillin, Cloxacillin, Tazobactam, Cephalexin, Cefadroxil, Cefaclor, Cefuroxime, Cefixime, Cefotaxime, Cefoperazone, Ceftazidime, Ceftizoxime, Ceftriaxone, Cefepime, Nalidixic acid, Ciprofloxacin, Lomefloxacin, Norfloxacin, Pefloxacin, Ofloxacin, Nitrofurantoin, Tetracycline, Co-trimaxazole, Clarithromycin, Roxithromycin, Erythromycin, Amikacin, Gentamicin, Tobramycin, Netilmicin, Kanamycin.

Data analysis was performed using the SPSS windows version 14.0 software. Tests of significance like Pearson's chi-square test and Fisher Exact test were applied to find out the results. A value of $P < 0.05$ was considered statistically significant.

Following Operational Definitions^[9] were put to use in the present study:

- Microscopy findings of more than 10 WBC per high power field were considered significant.
- Significant bacteriuria was defined as culture of a single bacterial species from the urine sample at a concentration of more than 100,000 cfu/ml.

Results

Five females suffering from diabetes mellitus, renal disorders, HIV positivity, or on corticosteroid therapy were also excluded. Two females who did not give

consent, were noncooperative or refused to provide the necessary information were not included in the study. Thus total number of females surveyed was 139. The overall prevalence of UTI was found to be 45.32% (95% confidence interval, 37.52–53.12). Overall 46.87% of 96 urban respondents and 41.86% of 43 rural respondents were identified with UTI. Thirty-two (51.61%) of 62 females aged between 25 and 34 years and 15 (46.87%) of 32 females aged between 15 and 24 years were identified with UTI. Ten (40.0%) of 25 females between 35 and 44 years and 6 (30.0%) of 20 females above 45 years of age had UTI. Five (26.31%) of 19 illiterate females were identified with UTI and 58 (48.33%) of 120 literate females had UTI. Fifty-six (44.09%) homemakers and six (66.67%) students were identified with UTI [Table 1].

The most common urinary symptom presented was burning micturition (73.4%) followed by frequency (43.9%), urgency (20.9%), painful voiding (20.1%), difficulty (5.0%), and nocturnal incontinence (1.4%).

Ten (50.0%) of 20 pregnant females had UTI compared to 53 (44.53%) of 119 nonpregnant females.

Out of the 63 pathogens, *E. coli* (33.1%) was the most common organism isolated followed by *Klebsiella pneumoniae* (7.9%), *Staphylococcus aureus* (2.2%),

Streptococcus pneumoniae (1.4%), and *Proteus mirabilis* (0.7%), respectively.

The most effective antibiotic for the *E. coli* isolates observed was Nitrofurantoin (86.95%) followed by Amoxicillin (69.56%), Nalidixic acid (65.21%), and Cotrimoxazole (60.86%). High efficacy of Nitrofurantoin (90.90%) followed by Cotrimoxazole and Tetracycline (81.81%) both was observed against the *Klebsiella* isolates. Cephalexin, Cefaclor, Nalidixic acid, and Norfloxacin also showed similar higher efficacies (72.72%) for *Klebsiella* isolates. Amoxicillin, Ampicillin-Sulbactam, Cefixime, Pefloxacin, and Ciprofloxacin also showed similar susceptibilities (63.63%) for *Klebsiella* isolates. High susceptibility (100%) for Ampicillin, Nitrofurantoin, and Tetracycline was observed among the identified *Proteus* isolates. Cefixime and Nalidixic acid were highly effective (100.0%) for *Staphylococcus aureus*. Norfloxacin was also found effective (66.66%) for *Staphylococcus aureus* isolates. High susceptibility patterns to Nalidixic acid, Clarithromycin, Cotrimoxazole, Cefixime, Cephalexin, and Cefaclor (100.0%) followed by Nitrofurantoin (66.66%) among the *Streptococcus* isolates identified were observed. Ceftriaxone, Cefepime, Cefuroxime, Ceftizoxime, Gatifloxacin, Gentamicin, Tetracycline, and Erythromycin showed similar efficacies (50.0%) for *Streptococcus* isolates [Tables 2a and b].

Table 1: Distribution of respondents according to their socio-demographic and clinical characteristics

Socio-demographic and clinical characteristics	Total no. of females surveyed (n=139) No. (%)	No. of females identified with UTI (n=63) No. (%)	95% confidence intervals (CI)	
			Lower CI	Upper CI
Place of residence				
Urban	96 (69.07)	45 (46.87)	38.40	55.34
Rural	43 (30.93)	18 (41.86)	33.49	50.23
Age				
15–24 years	32 (23.02)	15 (46.87)	38.40	55.34
25–34 years	62 (44.60)	32 (51.61)	43.13	60.09
35–44 years	25 (17.98)	10 (40.0)	31.69	48.31
>45 years	20 (14.38)	6 (30.0)	22.23	37.77
Marital status				
Married	128 (92.08)	56 (43.75)	35.33	52.17
Unmarried	11 (7.92)	7 (63.63)	55.47	71.79
Religion				
Hindu	119 (85.62)	58 (48.73)	40.25	57.21
Muslim	20 (14.38)	5 (25.0)	17.65	32.35
Education				
Illiterate	19 (13.67)	5 (26.31)	18.84	33.78
Literate	120 (86.33)	58 (48.33)	39.85	56.81
Occupation				
Homemaker	127 (91.36)	56 (44.09)	35.67	52.51
Employed	3 (2.15)	1 (33.33)	25.33	41.33
Student	9 (6.47)	6 (66.67)	58.67	74.67
Pregnancy				
Pregnant	20 (14.38)	10 (50.0)	41.52	58.48
Nonpregnant	119 (85.61)	53 (44.53)	36.10	52.96

Discussion

It is stated that UTI is predominantly a disease of the females due to a short urethra and proximity to vestibule and the anal opening. In our study too, out of the 139 females studied, 63 (45.32%) females were found to be urine culture positive. Similar findings were reported by Khan *et al.*, in Aligarh.^[10] Forty five (46.87%) out of 96 urban respondents and 18 (41.86%) out of 43 rural respondents were identified with UTI in our study. This may be attributed to the higher levels of awareness and treatment seeking behavior in the urban respondents compared to the rural respondents.

In our study, the prevalence of UTI was higher among the females aged between 15 and 44 years compared to those aged above 45 years of age. More cases of UTIs were recorded among young and middle age patients

(20–49 years, 51.04%) by Akram *et al.*^[11] In another study by Farhat Ullah *et al.*, middle-aged patients accounted for 54.3% of UTI.^[12] A higher percentage of literate females were identified with UTI compared to the literate ones in the current study. This may be due to the high treatment seeking behavior of the infected literates compared to illiterate ones.

In the present study the most common urinary symptom presented was burning micturition followed by frequency, urgency, and painful voiding. Similar trends have been reported by Medina-Bambardo *et al.*^[5]

The percentage of pregnant females with UTI was found to be slightly higher than the nonpregnant infected females in our study. This is similar to the study by Khan *et al.*, where out of 61 infected young women, 52 (86.8%) were found in their early or late phases of pregnancy.^[10]

Table 2a: Antibiotic susceptibility trends observed among the identified bacterial species causing urinary tract infection

Antibiotic against which susceptibility was observed	Bacterial species identified					P value
	<i>E. Coli</i> (n=46)	<i>Klebsiella</i> (n=11)	<i>Proteus</i> (n=1)	<i>S. aureus</i> (n=3)	<i>Streptococcus</i> (n=2)	
Penicillins						
Amoxicillin	32 (69.56)	7 (63.63)	0 (0.0)	0 (0.0)	0 (0.0)	0.163
Ampicillin	22 (47.82)	6 (54.54)	1 (100.0)	1 (33.33)	0 (0.0)	
Ampicillin-Sulbactam	12 (26.08)	7 (63.63)	0 (0.0)	0 (0.0)	0 (0.0)	
Piperacillin	1 (2.17)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	
Cloxacillin	1 (2.17)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	
Tazobactam	1 (2.17)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	
Cephalosporins						
1 st gen						
Cephalexin	19 (41.30)	8 (72.72)	0 (0.0)	1 (33.33)	2 (100.0)	1.000
Cefadroxil	5 (10.86)	2 (18.18)	0 (0.0)	0 (0.0)	0 (0.0)	
2 nd gen						
Cefaclor	16 (34.78)	8 (72.72)	0 (0.0)	1 (33.33)	2 (100.0)	1.000
Cefuroxime	12 (26.08)	5 (45.45)	0 (0.0)	0 (0.0)	1 (50.0)	
3 rd gen						
Cefixime	18 (39.13)	7 (63.63)	0 (0.0)	3 (100.0)	2 (100.0)	0.962
Cefotaxime	2 (4.34)	1 (9.09)	0 (0.0)	0 (0.0)	0 (0.0)	
Cefoperazone	4 (8.68)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	
Ceftazidime	1 (2.17)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	
Ceftizoxime	10 (21.73)	1 (9.09)	0 (0.0)	0 (0.0)	1 (50.0)	
Ceftriaxone	10 (21.73)	4 (36.36)	0 (0.0)	1 (33.33)	1 (50.0)	
4 th gen						
Cefepime	13 (28.26)	3 (27.27)	0 (0.0)	1 (33.33)	1 (50.0)	n.a
Fluoroquinolones						
Nalidixic acid	30 (65.21)	8 (72.72)	0 (0.0)	3 (100.0)	2 (100.0)	n.a
Ciprofloxacin	18 (39.13)	7 (63.63)	0 (0.0)	1 (33.33)	0 (0.0)	
Lomefloxacin	9 (19.56)	2 (18.18)	0 (0.0)	1 (33.33)	0 (0.0)	
Norfloxacin	23 (50.0)	8 (72.72)	0 (0.0)	2 (66.66)	0 (0.0)	
Pefloxacin	24 (52.17)	7 (63.63)	0 (0.0)	1 (33.33)	0 (0.0)	
Ofloxacin	7 (15.21)	1 (9.09)	0 (0.0)	0 (0.0)	0 (0.0)	

Figures in parenthesis are in percentage; n.a: Not applicable

Table 2b: Antibiotic susceptibility trends observed among the identified bacterial species causing urinary tract infection

Antibiotic against which susceptibility was observed	Bacterial species identified					P-value
	<i>E. coli</i> (n=46)	<i>Klebsiella</i> (n=11)	<i>Proteus</i> (n=1)	<i>S. aureus</i> (n=3)	<i>Streptococcus</i> (n=2)	
Nitrofurantoin	40 (86.95)	10 (90.90)	1 (100.0)	2 (66.66)	1 (50.0)	n.a.
Cotrimoxazole	28 (60.86)	9 (81.81)	0 (0.0)	1 (33.33)	2 (100.0)	n.a.
Tetracyclines	23 (50.0)	9 (81.81)	1 (0.0)	0 (0.0)	1 (50.0)	n.a.
Macrolide						
Clarithromycin	8 (17.39)	5 (45.45)	0 (0.0)	0 (0.0)	2 (100.0)	0.593
Roxithromycin	2 (4.34)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	
Erythromycin	17 (36.95)	6 (54.54)	0 (0.0)	0 (0.0)	1 (50.0)	
Amino glycosides						
Amikacin	2 (4.34)	1 (9.09)	0 (0.0)	0 (0.0)	0 (0.0)	0.982
Gentamicin	21 (45.65)	6 (54.54)	0 (0.0)	1 (33.33)	1 (50.0)	
Tobramycin	7 (15.21)	1 (9.09)	0 (0.0)	0 (0.0)	0 (0.0)	
Netilmicin	3 (6.52)	1 (9.09)	0 (0.0)	0 (0.0)	0 (0.0)	
Kanamycin	2 (4.34)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	

Figures in parenthesis are in percentage; n.a: Not applicable

Table 3: Distribution of pathogens isolated among UTI patients

Author and year of study	Percentage of bacterial species isolated				
	<i>E. coli</i>	<i>Klebsiella</i>	<i>Proteus</i>	<i>S. aureus</i>	<i>Streptococcus</i>
Babypadmini S <i>et al.</i> (2004) ^[13]	49.37	8.1	-	-	-
Mathai E <i>et al.</i> (2004) ^[14]	50.3	8.2	-	5.6	14.8
Khan AU <i>et al.</i> (2006) ^[10]	61	-	-	-	-
Tambekar DH <i>et al.</i> (2006) ^[7]	59	10	9	6	-
Akram M <i>et al.</i> (2007) ^[11]	61	22	-	7	-
Hasan AS <i>et al.</i> (2007) ^[15]	50.7	27.6	8.0	1.5	-
Selvakumar BN <i>et al.</i> (2007) ^[16]	44.02	14.53	0.64	-	-
Kothari A <i>et al.</i> (2008) ^[17]	68	16.9	5.5	-	-
Ramesh N <i>et al.</i> (2008) ^[18]	30.26	22.06	6.7	5	-
Present study	33.1	7.9	0.7	2.2	1.4

E. coli and *Klebsiella pneumoniae* were the most common organisms isolated in our study. These findings agree with other recent Indian reports which have indicated that gram-negative bacteria, mostly *E. coli* and *Klebsiella pneumoniae*, are the most common pathogens isolated in patients with UTI [Table 3].

The most effective antibiotic for *E. coli* in this study observed was Nitrofurantoin followed by Amoxicillin, Nalidixic acid, and Co-trimaxazole. This is similar to recent studies in India [Table 4]. The antimicrobial susceptibility pattern of *E. coli* varies widely by region. High efficacy of Nitrofurantoin followed by Co-trimaxazole and Tetracycline both was observed against *Klebsiella* in this study. Cephalixin, Cefclor, Nalidixic acid, Norfloxacin, Amoxicillin, Ampicillin-Sulbactam, Cefexime, Pefloxacin, and Ciprofloxacin were also effective for *Klebsiella*. Similar trends were reported by Kothari *et al.*, and Savas *et al.*^[17,19] However *Klebsiella* isolates showed higher susceptibility against

Imipenem (88%) and Amikacin (59%) in the study by Akram *et al.*^[11]

High susceptibility for Ampicillin, Nitrofurantoin, and Tetracycline was observed among the identified *Proteus* isolates in our study, whereas *Proteus spp.* showed the highest sensitivity to Ciprofloxacin (71.2%) in the study by Kashef *et al.*, in Iran.^[24] The present study revealed that Cefexime and Nalidixic acid were highly effective for *Staphylococcus aureus*. Whereas, all *Staphylococcus aureus* isolates were found to be susceptible against Imipenem, Ceftriaxone, and Cefotaxime by Akram *et al.*^[11] *Streptococcus* was found susceptible to Nalidixic acid, Clarithromycin, Cotrimaxazole, Cephalosporins, Nitrofurantoin, Gatifloxacin, Gentamicin, Tetracycline, and Erythromycin in our study. High susceptibility to aminoglycosides was also obvious in the study by Adedeji *et al.*, in Yola.^[25]

As we could not find similar studies, we used references

Table 4: Regional antibiotic susceptibilities of *E. coli* isolates

Author, year and place of study	Percentage of <i>E. coli</i> isolates susceptible to antibiotics													
	Gentamicin	Amikacin	Amoxicillin	Ampicillin	Amoxycillin clavulanic acid	Norfloxacin	Ciprofloxacin	Cotrimoxazole	Nitrofurantoin	Piperacillin tazobactam	Cephalosporins ES XP TE EC NT DR EU DM	Imipenem	Meropenem	
Mathai <i>et al.</i> (2004) ^[14] India*	82	-	-	54	-	-	79	50	90	-	89	-	-	
Khan <i>et al.</i> (2006) ^[10] India**	-	-	-	-	-	-	-	-	-	-	-	-	-	
Savas <i>et al.</i> (2006) ^[19] Turkey***	48.5	76.5	-	-	55.9	55.9	54.4	42.6	-	-	42.6-72.1	100	100	
Andrade <i>et al.</i> (2006) ^[20] L.America**	-	-	-	46.2	-	-	77.4	59.6	-	-	98.3-98.5	46.2	46.2	
Akram <i>et al.</i> (2007) ^[11] India**	-	49.0	-	-	-	-	-	-	-	-	15-45	100	-	
Tamayo <i>et al.</i> (2007) ^[21] Spain**	81.3	99.3	-	-	56.3	-	15.5	37.3	-	77.1	-	100	-	
Kiffer <i>et al.</i> (2007) ^[22] Brazil**	97	-	-	56.6	-	-	-	66.3	97.1	-	99.7	-	-	
Gobernado <i>et al.</i> (2007) ^[23] Spain**	-	-	-	47.6	94.3	80.7	81.4	74.1	66.6	-	95.5	-	-	
Kothari <i>et al.</i> (2008) ^[17] India**	-	75.6	17.7	-	41.6	-	35.8	30	65.7	99.888890.2	-	-	100	
Farhat Ullah <i>et al.</i> (2009) ^[12] Pakistan***	48.3	-	-	11.2	-	-	35.3	17.3	-	-	30.2 – 38	98.3	97.4	
Kashef <i>et al.</i> (2010) ^[24] Iran**	-	-	-	-	-	-	68.1	38.2	71.3	-	-	-	-	
Present study	45.6	4.34	69.5	47.8	-	50	39.1	60.8	86.9	4.34	2.1-39.1	2.1	-	

*UTI in pregnancy; **Community acquired UTI; ***Nosocomial UTI

of different field populations to compare our results. Those who visited Gynaecology consultation may have a different pretest probability of UTI than those who attended other hospital services or general practice consultations, and microbiological results can be also different.

Conclusions

This reflects the need for accurate and updated population surveillance data, particularly in light of concerns regarding variable regional antimicrobial susceptibility patterns. This information will directly affect selection of empiric therapy for UTI. Regular monitoring is required to establish reliable information about susceptibility pattern of urinary pathogens for optimal empirical therapy of patients with UTIs. We suggest that empirical antibiotic selection should be based on the knowledge of local prevalence of bacterial organisms and antibiotic sensitivities rather than on universal guidelines. IEC messages for all the UTI patients must include the additional information about the risk reduction methods and need to take regular supervised treatment.

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